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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,342	09/18/2000	Rudi Brands	01975.0025	8325

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09/20/2002

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EXAMINER

LI, BAO Q

ART UNIT

PAPER NUMBER

1648

DATE MAILED: 09/20/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/582,342

Applicant(s)

BRANDS, RUDI

Examiner

Bao Qun Li

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1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 19 July 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 7-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2 and 7-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Claims 1-2, 7-26 are pending.

### ***RCE***

The request filed on 07/19/2002 for a request for continued examination (RCE) under 37 CFR 1.114 (d) based on parent Application No. 09/582,342 is acceptable and a RCE has been established. An action on the RCE follows.

### ***Response to Amendment***

This is a response to the amendment, paper No. 19, filed 07/17/02. Claims 1, 2, 10 and 25 are amended. Claims 1-2 and 7-26 are pending before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

### ***New Matter***

The amendment filed 07/17/2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: “ b) dividing the cells of the preproduction batch at least two separate batch.

Applicant is required to cancel the new matter in the reply to this Office Action.

### ***Claim Rejections - 35 USC § 102***

Claims 1-2, 9-22 and 26 are still rejected under 35 U.S.C. 102 (b) over the prior art of Griffiths,s document, on the same grounds as previously stated in the Office Action mailed 12/03/2001.

Applicant submitted that the claims are amended and that rejection is improper because Griffiths does not describe either expressly or inherently the claimed invention.

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Applicant's argument as part of amendment C, and amended claims Paper NO. 19, filed 07/17/02, have been considered fully, but they are not persuasive because Griffiths teaches all general principle (See section 2 on pages 59-60) and steps of scale-up culturing both suspension (See section 3.1 on pages 62-65) and anchorage-dependent cells (See section 3.2, on pages 60-74). For example, Griffiths et al. state that the scale-up of cell culture is described in a laboratory context (10-20L), but the principles and techniques employed have been successfully adapted so that cells are now grown in industrially in unit volumes of up to 10,000 L for vaccine, interferon and monoclonal antibody production. This has allowed the use of faster growing and less fastidious cell lines, such as CHO, and amplification of product expression by multiple copies of the gene (lines 1-18 on page 59). They also explicitly teach some of the steps of suspension culture as prewarming to 37°C, and equilibrating the pH of the culture medium with CO<sub>2</sub>/air gas mix, before inoculating the cells, inoculating cells at over  $1 \times 10^5$ /ml or at  $2-3 \times 10^5$ /ml for many hybridoma cell lines, stirring the culture at 100-300 rpm, monitoring the cell growth daily and harvesting cell or maintaining the cells with fresh medium after the cells reach to the stationary phase in 3-4 days (See section 3.1.2. on pages 62-63). Griffiths et al. also teach some special procedure for culturing the cells in an anchorage dependent manner, such as use of hollow-fiber cartridges (See section of 3.1.3..2 on pages 63-65) and Cytodex 3 microcarrier at 3-15 g/L (pp. 67-71, section 3.2.1.3. and 3.2.2). Griffiths et al. also teach attachment of cells by first washing the cells with PBS and then treating with trypsin/EDTA (pp. 67, step 6 and pp. 71, step 7). Griffiths et al. taught that during the second step of the scale-up culture, the cell density/unit volume increase 10-100 time, in another word, at the begging of the culture, the cell population is only 10% of the final volume of the culture (pp. 60, lines 2-5). While the statement of Griffiths' teaching words differently from the claims, they teaches all steps of the claimed invention including culturing the suspension or anchorage dependent cell to form a preproduction batch or dividing the cells to separate batch for either producing one biological or as seed for the preparation of at least one subsequent preproduction batch. Therefore, the rejection is till proper and maintained.

Applicant further reminded that the Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the

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objections made. Further, they do not show how the amendments avoid such references or objections.

***Claim Rejections - 35 USC § 103***

Claims 1-2 and 7-26 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (Scale-up of suspension and Anchorage-dependent Animal cells in Basic Cell Culture Protocols, Edited by Pollard et al. Humana Press Inc., 1997, pp.59-75), and Pollard (Basic Cell Culture Protocols, Edited by Pollard et al. Humana Press Inc., 1997, Step 14-20 on page 3 and Section 3.2 on page 4-5).

Applicant argues that the rejection is improper because the combination of these references does not teach or suggest the claimed invention or when combined, the cited references must teach or suggest all the claimed limitations.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that the obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the present invention is drawn to a method of scale-up cell culture in industry for producing the biological molecules, the general steps for starting a cell culture, splitting the cell culture in certain ratios according to the demanded usage, and maintaining the cell culture in a healthy condition are all taught by Griffiths. The detail procedure for freezing cells for later use as told by Griffiths and Pollard is a common procedure, which is a routine method available in the art. Although the claims are amended to dividing cells into at least two batches, one batch is used for production and another batch is seeded for subsequent preparation, the modification of the splitting cells in different ratios is generally recognized as being within the level of the ordinary skill in the art, *In re Rose*, 105 USPQ 237 (CCPA 1995) because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the workable ranges involves only routine skill in the art, *In re Aller*, 105, USPQ 233.

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Hence, it is still concluded that the rejection is maintained since the claimed invention as a whole is prima facie obvious absence unexpected results. The rejection

**New Ground of Rejection:*****Claim Rejections - 35 USC § 112***

Claims 1-2 and 7-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The original specification was silent as to dividing cells of the preproduction batch into at least two separate batches. According to page 2, line 4 and line 11 of the instant application, such procedure is disclosed as at least one production batch. Please provide the support in the specification to overcome the new matter rejection.

***Claim Rejections - 35 USC § 102***

Claims 1-2, 9, 11-14, 22, and 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al. (Hollow-Fiber Cell Culture in Basic Cell Culture protocols, Edited by Pollard et al. Humana Press Inc, 1997, pp. 77-89).

Davis et al. taught a system of Hollow-Fiber cell culture system, wherein the cells can be anchorage-dependent cells and the starting population of the cells ( $2 \times 10^6/\text{ml}$ ) is 10-20% of final concentration of the cells ( $8 \times 10^6/\text{ml}$  to  $2 \times 10^8/\text{ml}$ ) (pp. 83-84, section 3.3). Davis et al. also taught that the said cultured cells can be frozen according to standard procedure in the art and be used by next time (pp. 87, step 10). Therefore, the cited referenced is inherent by the claimed invention.

Previously, applicants argued that Davis's reference does not teach that the cell culture system is a repeated discontinuous process, since this limitation has been withdrawn in the newly submitted amendment, the rejection is resumed.

***Conclusion***

No claims are allowed.

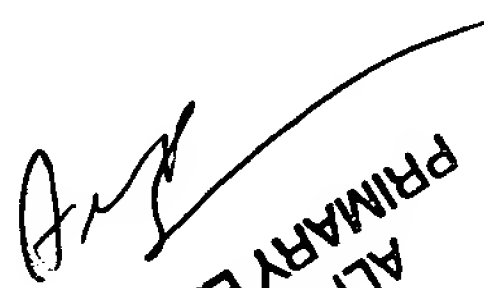
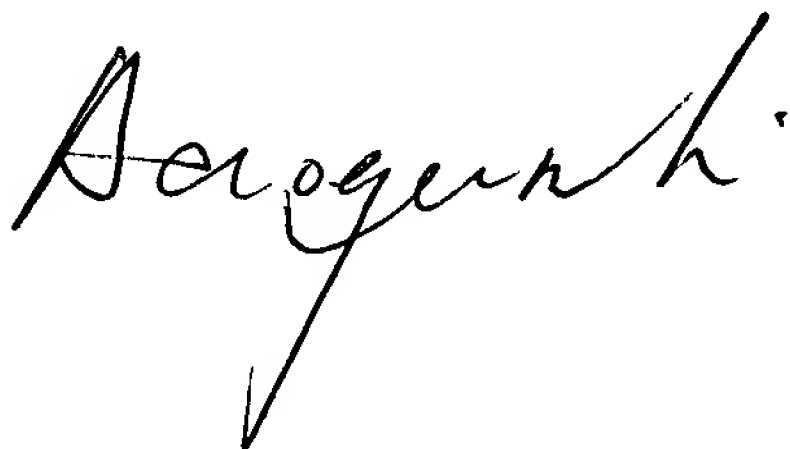
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

September 18, 2002



ALI R. SALIMI  
PRIMARY EXAMINER